



Lecture 4

Oxytocics & tocolytics

Objectives:

- ★ Drugs used to induce & augment labor.
- ★ Drugs used to control postpartum hemorrhage.
- ★ Drugs used to induce pathological abortion.
- ★ Drugs used to arrest premature labor.
- ★ The mechanism of action and adverse effects of each drug.

- Additional Notes
- **Important**
- Explanation –Extra-

Oxytocin (Syntocinon)

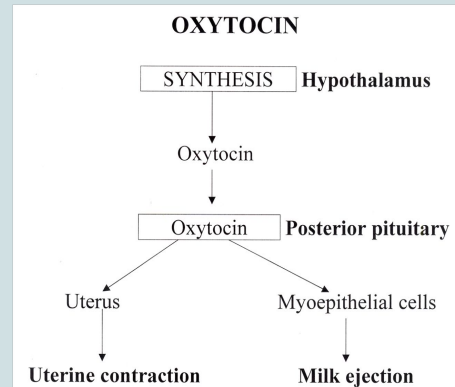
Role of oxytocin:

On Uterus

- Stimulates both the frequency and force of uterine contractility **particularly of the fundus** segment of the uterus.
- These contractions resemble the normal physiological contractions of uterus (**contractions followed by relaxation**)
- Immature uterus is resistant to oxytocin. **Just in full term**
- Contract uterine smooth muscle only at term.
- Sensitivity increases to 8 fold in last 9 weeks and 30 times in early labor.
- Clinically oxytocin is given only when uterine cervix is **soft** and **dilated**.

On Myo-epithelial cells

- Oxytocin contracts myoepithelial cells surrounding mammary alveoli in the breast & leads to **milk ejection**.



Pharmacokinetic S

- Not effective orally (**destroyed in GIT**)
- Also as nasal spray (**impaired milk ejection**)
- Catabolized by liver & kidneys
- Administered i.v. (augment labor)
- Not bound to plasma proteins
- Half life = **5 minutes**

MOA

- The interaction of endogenous or administered oxytocin, with myometrial cell membrane receptor promotes the **influx of Ca^{++} from extracellular fluid and from S.R (Sarcoplasmic reticulum) into the cell, this increase in cytoplasmic calcium, stimulates uterine contraction.**

Uses

- 1. Induction & augmentation of labor** (at full term & dilated cervix) (it is used to cause contraction of the uterus in order to start labor or increase the speed of labor, and to stop bleeding following delivery). (**slow I.V infusion**)
 - a) Mild preeclampsia تسمم حمل near term
 - b) Uterine inertia (the women in labor but the uterine shows no contraction)
 - c) Incomplete abortion
 - d) Post maturity
 - e) Maternal diabetes
- 2. Post partum uterine hemorrhage** (نزيف بعد الولادة)
(**I.V drip**) (**ergometrine is often used** very strong contraction of smooth muscles and closure of blood vessels)
- 3. Impaired milk ejection**
One puff in each nostril 2-3 min before nursing

Side Effects

1. Maternal death due to hypertension
2. Uterine rupture
3. Fetal death (ischemia)
4. Water intoxication (Convulsions and coma) if oxytocin is given with relatively large volumes of electrolyte-free aqueous fluid intravenously

Contraindications

- a) Hypersensitivity
- b) Prematurity
- c) Abnormal fetal position
- d) Evidence of fetal distress
- e) Cephalopelvic disproportion
- f) Incompletely dilated cervix

Precautions

- a) Multiple pregnancy
- b) Previous c- section
- c) Hypertension

Ergot Alkaloids

Natural: Ergometrine (Ergonovine)

Synthetic: Methylergometrine (Methylergonovine)

Effects on the Uterus

- Ergot alkaloids induce **TETANIC CONTRACTION** of uterus without relaxation in between (not like normal physiological contractions)
- It causes contractions of uterus as a whole i.e. fundus and cervix (tend to compress rather than to expel the fetus)

pharmacokinetics

- Usually given I.M
- Extensively metabolized in liver
- 90% of metabolites are excreted in bile

Clinical uses	Postpartum hemorrhage (3rd stage of labor)
Preparations	Syntometrine (oxytocin with ergometrine) (ergometrine 0.5 mg + oxytocin 5.0 I.U) , I.M.
Side effects	a) Nausea, vomiting, diarrhea b) Hypertension b) Vasoconstriction of peripheral blood vessels (toes & fingers) c) Gangrene
Contraindications	1) Induction of labour a) 1 st and 2 nd stage of labor b) vascular disease c) Severe hepatic and renal impairment d) Severe hypertension

PROSTAGLANDINS

<p>Drugs</p>	<p>PGE₂ – Dinoprostone (Given as Vaginal suppository. Or Given extra-amniotically as a solution.)</p>	<p>PGF₂α- Dinoprost, Carboprost (Given as intra-amniotic injection)</p>	<p>Misoprostol (synthetic PGE₁) (Given intravaginally as a gel or tablet)</p>
<p>Therapeutic uses</p>	<ol style="list-style-type: none"> 1. Induction of abortion (pathological) 2. Induction of labor (fetal death in utero) 3. Postpartum hemorrhage 		
<p>Side Effects</p>	<ul style="list-style-type: none"> - Nausea , vomiting - Abdominal pain - Diarrhea - Bronchospasm (PGF₂α) - Flushing (PGE₂) 		
<p>Contraindications</p>	<ol style="list-style-type: none"> 1- Mechanical obstruction of delivery 2- Fetal distress خاصة لما تكون الام كبيرة 3- Predisposition to uterine rupture 		
<p>Precautions</p>	<ul style="list-style-type: none"> - Asthma - Multiple pregnancy - Glaucoma - Uterine rupture 		

Difference B/w Oxytocin and Prostaglandins and Ergometrine

Character	Oxytocin	Prostaglandins	Ergometrine
Contraction	<ul style="list-style-type: none"> -Only at term . -Resembles normal physiological contractions 	<ul style="list-style-type: none"> - Contraction throughout pregnancy 	<ul style="list-style-type: none"> -Tetanic contraction ; doesn't resemble normal physiological contractions
Cervix	Does not soften the cervix	soften the cervix	-
Duration of action and onset of action	<ul style="list-style-type: none"> -Rapid onset -Shorter duration of action 	<ul style="list-style-type: none"> -longer duration of action 	<ul style="list-style-type: none"> -moderate onset -long duration of action
Uses	<ul style="list-style-type: none"> -Induce and augment labor postpartum hemorrhage 	<ul style="list-style-type: none"> -Induce abortion in 2nd trimester of pregnancy. -Used as vaginal suppository for induction of labor 	<ul style="list-style-type: none"> -Only in postpartum hemorrhage

Tocolytic Drugs “Drugs Producing Uterine Relaxation”

Relax the uterus and arrest threatened abortion or delay premature labor.

<p>Drugs</p>	<p>1. β-ADRENOCEPTOR AGONISTS *Ritodrine Given i.v. drip</p>	<p>2. CALCIUM CHANNEL BLOCKERS *Nifedipine</p>	<p>3. Atosiban Given by IV infusion for 48 hrs</p>
<p>MOA</p>	<p>- Bind to β-adrenoceptors \rightarrow activate enzyme Adenylate cyclase \rightarrow increase in the level of cAMP \rightarrow reducing intracellular calcium level.</p>	<p>- Markedly inhibits the amplitude of spontaneous and oxytocin-induced contractions</p> <p>- Causes relaxation of myometrium</p>	<p>-Compete with oxytocin at its receptors on the uterus.</p> <p>- New tocolytic agent</p>
<p>Side effects</p>	<ul style="list-style-type: none"> •Tremor •Nausea , vomiting •Flushing •Sweating •Tachycardia *high dose •Hypotension •Hyperglycemia •Hypokalaemia 	<ul style="list-style-type: none"> •Headache, dizziness • Hypotension • Flushing •Constipation • Ankle edema • Coughing • Wheezing • Tachycardia 	

MCQs

Q1/Which one of the following is the effect of oxytocin on the uterus?

- A-relaxation
- B-contraction
- C-dilation
- D-no effect

Q2/Ergote is contraindicated in which stage of labor?

- A-first stage
- B-second stage
- C-third stage
- D-first and second stages

Q3/Which one of the following is the action of Atosiban :

- A. depletion of prostaglandins
- B. Compete with oxytocin at its receptors on the uterus
- C. Bind to β -adrenoceptors

Q4/Prostaglandin induced abortion in which trimester:

- A-first
- B-second
- C-third
- D-all

Q5/ Which one is β -agonist and used as tocolytic drug?

- A-ritodrine
- B- Atosiban
- C- Aspirin
- D- celecoxib

Q6/ 28 year old female came to the clinic complaining of spontaneous uterine contractions which of the following is the best drug for treatment ?

- A. Oxytocin
- B. aspirin
- C. Atosiban
- D. Nifedipine

Good luck!

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